

WHAT IS CLAIMED IS:

1. A stable tablet formulation comprising an initial amount of a crystalline polymorph, designated polymorph B, of (6R)-L-erythro-tetrahydrobiopterin and a pharmaceutically acceptable excipient, wherein after six months at room temperature and about 60% humidity the stable tablet formulation retains at least about 95% of the initial amount of (6R)-L-erythro-tetrahydrobiopterin, and wherein said crystalline polymorph, as a hydrochloride salt, exhibits an X-ray powder diffraction pattern with the following characteristic peaks expressed in d-values(A) : 8.7 (vs), 5.63 (m), 4.76(m), 4.40 (m), 4.00 (s), 3.23 (s), 3.11 (vs), preferably 8.7 (vs), 6.9 (w), 5.90 (vw), 5.63 (m), 5.07 (m), 4.76 (m), 4.40 (m), 4.15 (w), 4.00 (s), 3.95 (m), 3.52 (m), 3.44 (w), 3.32 (m), 3.23 (s), 3.17 (w), 3.11 (vs), 3.06 (w), 2.99 (w), 2.96 (w), 2.94 (m), 2.87 (w), 2.84 (s), 2.82 (m), 2.69 (w), 2.59 (w), and 2.44 (w).
2. The stable tablet formulation of claim 1, wherein after nine months at room temperature and about 60% humidity the stable tablet formulation retains at least about 95% of the initial amount of (6R)-L-erythro-tetrahydrobiopterin.
3. The stable tablet formulation of claim 1 or 2, wherein the stable tablet formulation retains at least about 98% of the initial amount of (6R)-L-erythro-tetrahydrobiopterin.
4. The stable tablet formulation of claim 1, wherein the initial amount of (6R)-L-erythro-tetrahydrobiopterin is in the range of about 30 wt% to about 40 wt% of the formulation.
5. The stable tablet formulation of claim 1, wherein the initial amount of (6R)-L-erythro-tetrahydrobiopterin is in the range of about 32 wt% to about 35 wt% of the formulation.
6. The stable tablet formulation of claim 1, wherein the initial amount of (6R)-L-erythro-tetrahydrobiopterin is in the range of about 33 wt%.
7. The stable tablet formulation of any of claims 1-5, wherein the initial amount of (6R)-L-erythro-tetrahydrobiopterin in each tablet is about 100 mg.

8. The stable tablet formulation of any of claims 1-5, wherein the initial amount of (6R)-L-erythro-tetrahydrobiopterin in each tablet is about 200 mg.

9. The stable tablet formulation of any of claims 1-8, further comprising a binder.

10. The stable tablet formulation of claim 9, wherein the binder is anhydrous dibasic calcium phosphate.

11. The stable tablet formulation of any of claims 9-10, wherein the binder is in the range of about 1 wt% to about 5 wt%.

12. The stable tablet formulation of any of claims 9-10, wherein the binder is in the range of about 1.5 wt% to about 3 wt%.

13. The stable tablet formulation of any of claims 9-12, wherein the weight ratio of binder to tetrahydrobiopterin is in the range of about 1:10 to about 1:20.

14. The stable tablet formulation of claim 13, wherein the weight ratio of binder to tetrahydrobiopterin is about 1:15.

15. The stable tablet formulation of any of claims 1-14, further comprising a disintegration agent.

16. The stable tablet formulation of claim 15, wherein the disintegration agent is crospovidone.

17. The stable tablet formulation of any of claims 15-16, wherein the disintegration agent is in the range of about 3 wt% to about 10 wt%.

18. The stable tablet formulation of claim 17, wherein the disintegration agent is in the range of about 3 wt% to about 5 wt%.

19. The stable tablet formulation of any of claims 1-18, wherein the weight ratio of disintegration agent to tetrahydrobiopterin is in the range of about 1:5 to about 1:10.

20. The stable tablet formulation of claim 19, wherein the weight ratio of disintegration agent to tetrahydrobiopterin is about 1:7.5.

21. The stable tablet formulation of any of claims 1-20, further comprising an acidic antioxidant.

22. The stable tablet formulation of claim 21, wherein the acidic antioxidant is ascorbic acid.

23. The stable tablet formulation of any of claims 21-22, wherein the acidic antioxidant is in the range of about 1 wt% to about 3 wt%.

24. The stable tablet formulation of any of claims 1-23, wherein the weight ratio of acidic antioxidant to tetrahydrobiopterin is in the range of about 1:5 to 1:30.

25. The stable tablet formulation of claim 24, wherein the weight ratio of acidic antioxidant to tetrahydrobiopterin is about 1:20.

26. The stable tablet formulation of any of claims 1-25, further comprising a lubricant.

27. The stable tablet formulation of claim 26, wherein the lubricant is stearyl fumarate.

28. The stable tablet formulation of any of claims 25-26, wherein the lubricant is in the range of about 0.1 wt% to about 2 wt%.

29. The stable tablet formulation of claim 28, wherein the lubricant is in the range of about 0.5 wt% to about 1 wt%.

30. The stable tablet formulation of any of claims 1-29, wherein the weight ratio of lubricant to tetrahydrobiopterin is in the range of about 1:25 to 1:65.

31. The stable tablet formulation of claim 30, wherein the weight ratio of lubricant to tetrahydrobiopterin is about 1:45.

32. The stable tablet formulation of any of claims 1-31, further comprising vitamin B2 (riboflavin).

33. The stable tablet formulation of any of claims 1-32, further comprising vitamin B12.

34. The stable tablet formulation of any of claims 1-33, further comprising a folate.

35. The stable tablet formulation of any of claims 1-34, further comprising arginine.

36. The stable tablet formulation of claim 34, wherein the folate is folic acid (pteroylmonoglutamate), dihydrofolic acid, tetrahydrofolic acid, 5-methyltetrahydrofolic acid, 5,10-methylenetetrahydrofolic acid, 5,10-methenyltetrahydrofolic acid, 5,10-formiminotetrahydrofolic acid, 5-formyltetrahydrofolic acid (leucovorin), 10-formyltetrahydrofolic acid, 10-methyltetrahydrofolic acid, a folylpolyglutamates, a dihydrofolate, a tetrahydrofolates, 5-formyl-(6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid or (6S)-tetrahydrofolic acid, or pharmaceutically acceptable salts thereof.

37. A stable tablet formulation of (6R)-L-erythro-tetrahydrobiopterin, comprising an initial amount of a crystalline polymorph of (6R)-L-erythro-tetrahydrobiopterin in the range of about 32 wt% to about 35 wt% of the formulation, crospovidone in the range of about 3 wt% to about 5 wt%, anhydrous dibasic calcium phosphate in the range of about 1.5 wt% to about 3 wt%, and stearyl fumarate in the range of about 0.5 wt% to about 1 wt%,

wherein said stable tablet formulation has a shelf life at room temperature of at least 6 months, and

wherein said crystalline polymorph, as a hydrochloride salt, exhibits an X-ray powder diffraction pattern with the following characteristic peaks expressed in d-values(A) : 8.7 (vs), 5.63 (m), 4.76(m), 4.40 (m), 4.00 (s), 3.23 (s), 3.11 (vs), preferably 8.7 (vs), 6.9 (w), 5.90 (vw), 5.63 (m), 5.07 (m), 4.76 (m), 4.40 (m), 4.15 (w), 4.00 (s), 3.95 (m), 3.52 (m), 3.44 (w), 3.32 (m), 3.23 (s), 3.17 (w), 3.11 (vs), 3.06 (w), 2.99 (w), 2.96 (w), 2.94 (m), 2.87 (w), 2.84 (s), 2.82 (m), 2.69 (w), 2.59 (w), and 2.44 (w).

38. The stable tablet formulation of claim 37 which has a shelf-life at room temperature of at least nine months.

39. The stable tablet formulation of claim 37 or 38 wherein the initial amount of said crystalline polymorph of (6R)-L-erythro-tetrahydrobiopterin is

about 33 wt%, crospovidone is about 4.5 wt%, anhydrous dibasic calcium phosphate is about 2 wt%, and stearyl fumarate is about 0.75 wt%.

40. A method of making the stable tablet formulation of any one of claims 1-39 comprising the steps of mixing an initial amount of said crystalline polymorph of (6R)-L-erythro-tetrahydrobiopterin and one or more pharmaceutically acceptable excipients, and forming a tablet from the mixture, wherein the steps do not include adding liquid water.

41. The method of claim 40, wherein the one or more pharmaceutically acceptable excipients include a binder.

42. The method of claim 41, wherein the binder is anhydrous dibasic calcium phosphate.

43. The method of any of claims 1-42, wherein the one or more pharmaceutically acceptable excipients include a disintegration agent.

44. The method of claim 43, wherein the disintegration agent is crospovidone.

45. The method of any of claims 1-44, wherein the one or more pharmaceutically acceptable excipients include an acidic antioxidant.

46. The method of claim 45, wherein the acidic antioxidant is ascorbic acid.

47. The method of any of claims 1-46, wherein the one or more pharmaceutically acceptable excipients include a lubricant.

48. The method of claim 47, wherein the lubricant is formyl stearate.